

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
28 July 2005 (28.07.2005)

PCT

(10) International Publication Number
WO 2005/068649 A1

- (51) International Patent Classification⁷: **C12Q 1/68**
- (21) International Application Number:
PCT/EP2005/000337
- (22) International Filing Date: 14 January 2005 (14.01.2005)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/536,624 15 January 2004 (15.01.2004) US
60/613,012 23 September 2004 (23.09.2004) US
- (71) Applicant (for all designated States except US): **NOVARTIS FORSCHUNGSSTIFTUNG [CH/CH];** c/o Novartis International AG, Lichtstrasse 35, CH-4056 Basel (CH).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **CUENOD, Michel** [CH/CH]; Chemin de la Becque 42, CH-1814 La Tour-de-Peilz (CH). **DO-CUENOD, Kim, Quang** [CH/CH]; Chemin de la Becque 42, CH-1814 La Tour-de-Peilz (CH). **TOSIC, Mirjana** [CH/CH]; Avenue du Servan 11, CH-1006 Lausanne (CH).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **DIAGNOSTIC AND TREATMENT OF A MENTAL DISORDER**

(57) Abstract: The present invention generally relates to the field of neurological, physiological and psychotic dysfunctions associated with a mental disorder such as schizophrenia, or a predisposition therefor. The invention further relates to genes and proteins, which, when varied in their normal expression, their nucleic acid sequence or in their activity, are associated with the mental disorder. Accordingly, the present invention relates to methods for diagnosis and to methods for prevention and/or treatment of a mental disorder. The present invention additionally relates to compositions for use in diagnosis and to kits for diagnosis of a mental disorder. The invention also relates to the use of a protein or polynucleotide for the manufacture of a medicament for use in the treatment and/or prevention and to a pharmaceutical composition for use in prevention and/or treatment of a mental disorder. Further, the invention relates to methods for screening for a modulator of a mental disorder. More particularly, the present invention relates to methods, compositions and kits, a microarray and reagents for determining the presence of at least one polymorphism and/or at least one combination of polymorphisms of at least one copy of a gene involved in regulating the intracellular glutathione (GSH) level and/or GSH-oxidative stress-related gene expression in a human being. Further, the invention relates to a pharmaceutical composition for use in the treatment and/or prevention of a mental disorder, to the use of an active ingredient such as a protein or polynucleotide for the manufacture of a medicament for use in the treatment and/or prevention of a mental disorder in patients with specific polymorphisms in genes involved in regulating the intracellular GSH level and/or GSH-oxidative stress-related gene expression. The invention also relates to methods of preventing and/or treating a mental disorder comprising administering a medicament to patients having said polymorphisms and to methods of screening for a modulator of a mental disorder.

WO 2005/068649 A1